

FIG. 1A

CCGGGTCGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG
5 CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCCTCCCCTCTGTGTGGC
CGGAATCCTTGCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA
GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC
TAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCGGG
CTGCAGGCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA
10 GGCTCACCAGGAGGACACAGAGCGCTATGTGCTACCAACCTCAACATCGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG
CTGACCTGGTCTCTATATCACTAGTTTTGACCTGGAGTTGCCTGATGGTAACCGGCAG
15 GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATT
CCGAGGACACTGGCTTCGACCTGGGAGTCACCATTGCCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCACGACGGCGCGCCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA
TGGCTTCGGACGGCGCCGCGCCCCGCGCCGGCCTCGCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCCGC
20 GGCCTCAACCCGGGTCCGCGGGGCACCCGCCGGATGCGCAGCCTGGCCTCTACTACA
GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTGCGCTGCACCTTCGC
CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGCAGCCGCTCCTCGTTCTCCTGCTGATGGGACAGAATGTGGCGTGGAGA
AGTGGTGTCTCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCCATAGCAGCAGT
25 GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA
GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCAGACCTGCCTTTGGGGGGCGT
GCATGTGTTGGTGTGCTGACCTCCAGGCCGAGATGTGCAAACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTCATGTGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
CTCCCCTGGCGGCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG
30 GATGCTCTGTGCAGACACATGTGCCGGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG
GAGACAGCTTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCCGGGAGGACGGGA
CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTGGCTGTGATGGTAGGATGGA
CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGACAACAGCACGTGCAGC
CCACGGAAGGGCTCTTTACAGCTGGCAGAGCGAGAGAATATGTCAGTTTCTGACAGT
35 TACCCCCAACCTGACCAGTGTCTACATTGCCAACCACAGGCCTCTCTTCACACACTTGG
CGGTGAGGATCGGAGGGCGCTATGTCGTGGCTGGGAAGATGAGCATCTCCCCTAACAC
CACCTACCCCTCCCTCCTGGAGGATGGTGTGTCGAGTACAGAGTGGCCCTACCGAG

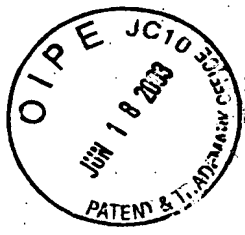


FIG. 1B

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAACTACAGCTGCCTG
5 GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCTGCGTGCTCGAACCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCCAGGGCAGCCTCCTGAAGACATTGCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAACCTGCAACCCCCAGCCCTGCCCTGCC
10 AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGAAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG
15 TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTGCTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT
20 GCCTCGCCCCGAACCCAGGAGGCCTGCAGCCTGGAGCCCTGCCACCTAGGTGGAA
AGTCATGTCCCTTGCCCCATGTTGCGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCTGTGGGGATGGCATCCAGCG
25 CCGGCGTGACACCTGCCTCGGACCCAGGCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCTCGGGGAGGT
30 GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGGGGGGACATGTTGCTG
CTTTGGGGCGCGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA
35 ATGCAGGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

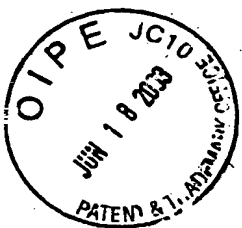


FIG. 1C

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

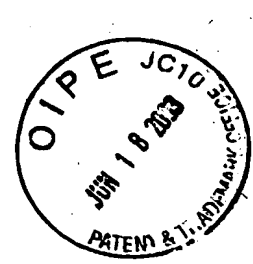


FIG. 2

5 PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLGCGWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRQRRRAAGGILHLELLVAVGPDVFAQHQED
TERYVLTNLNIGAELLRDP SLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTPDGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSPTW SCLITEDTGFDLGVTIAHEI
10 GHSFGLEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRLQLLSLLSAGRARCWWD
PRPQPGSAGHPPDAQPGLYYSANEOCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGV
TRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAPHSQGDALCRHMCRAIGESFIMKRGSFLDGT RCMPSGPREDGTL SLCVS
15 GSCRTFGCDGRMDSQQVWDR CQVCGDNSTCSPRKGSFTAGRAREYVTF LTVTPNLTSV
YIANHRPLFTHLAVRIGGRYV VAGKMSISPNTTYP SLLDGRVEYRVALTEDRLPRLEEIRIW
PLQEDADIQVYRRYGEEYGNL TRPDITFTYFQPKPRQAWVWA AAVRGPCSVSCGAGLRWN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARC RAGAQQPAVALET CNPQPCPARWEVSEPSSCTSAGGAGLAL
20 ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHWTPAAGSCSVSCGRGLMELRFLCMDSALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVRRILYCARAHGEDDGEI LLDTCQCGLP RPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLTARRSVACVQLDOGQDVEVDEAACAALVRPEASV
PCLADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPKPVTVRGC
25 WAGPCVGQGTPSLVPHEEAAAPGR TTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTN TLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

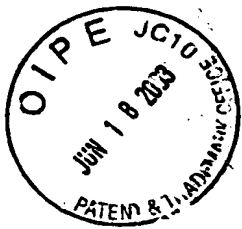
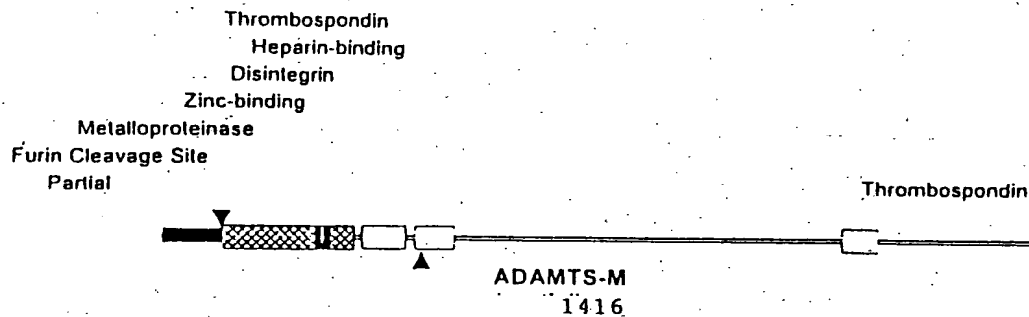


FIG. 3A

Domain structure of ADAMTS-M and translated nucleic acid sequence. FIG. 3A Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). FIGS. 3B-3G ADAMTS-M nucleotide sequence with translated amino acid sequence above.



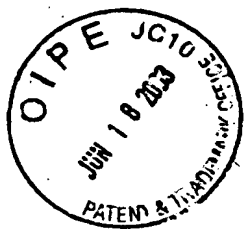


FIG. 3B

+1 P G R P T R P K A P S H S A P L L G L A L L R N H Q R

Partial Prodomain

25 CCGGGTCGAC CCACGCGTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGCACCAGCG
GGCCCAAGCTG GGTGCGCAGG CTTCCGGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCCG

+1 H P R A R C P P L C V A G I L A C G F L L G C W S F

Partial Prodomain

105 TCACCCCGG GCAAGATGCC CTCCTCTG TGTGGCCGGA ATCCTTGCCT GTGGCTTTCT CCTGGGCTGC TGGGGACCCG
AGTGGGGGCG CGTTCTACGG GAGGGGAGAC ACACCGGCT TAGGAACGGA CACCGAAAGA GGACCCGACG ACCCTGGGA

+1 S H F Q O S C L Q A L E P Q A V S S Y L S P G A P L K

Partial Prodomain

185 CCCATTTCCA GCAGAGTTGT CTTCAAGGCT TGGAGCCACA GGCGGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTAAAA
GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAACG CCGGACCACG AGGGAATTT

+1 G R P P S P G F Q R Q R Q R R A A G G I L H L E L

Furin Cleavage Site (Motif)

Partial Prodomain

Metalloproteinase Domain

265 GGCGGCCCTC CTTCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
CCGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA

+1 L V A V G P D V F Q A H Q E D T E R Y V L T N L N :

Metalloproteinase Domain

345 GCTGGTGGCC GTGGGCCCCG ATGCTTCCA GGCTCACCAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
CGACCACCG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCTGTGTCT TCGCGATACA CGAGTGGTTG GAGTTGTAGC

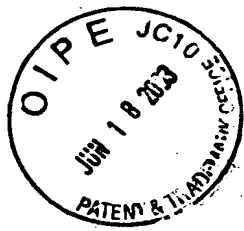


FIG. 3C

+1 G A E L L R D P S L G A Q F R V H L V K H V I L T E F
Metalloproteinase Domain

425 GGGCAGAACT GCTTCGGGAC CCGTCCCTGG GGGCTCAGTT TCGGGTGAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCACGCTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

+1 E G A P N I T A N L T S S L L S V C G W S Q T I N P E
Metalloproteinase Domain

505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCTTGA
CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT

+1 D D T D P G H A D L V L Y I T R F D L E L P D G N E
Metalloproteinase Domain

585 GGACGACAG GATCCTGGCC ATGCTGACCT GGTCCTCTAT ATCACTAGGT TTGACCTGGA GTTGCTGAT GGTAAACGGC
CCTGCTGTGC CTAGGACCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG

+1 Q V R G V T Q L G G A C S P T W S C L I T E D T G F E
Metalloproteinase Domain

665 AGGTGCGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCTCATT CCGAGGACAC TGGCTTCGAC
TCCACGCCCC GCAGTGGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCCTGTG ACCGAAGCTG

+1 L G V T I A H E I G H S F G L E H D G A P G S G C G F
Zinc-binding Motif

Metalloproteinase Domain

745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCC
GACCTCAGT GGTAACGGGT ACTCTAACC GTGTCGAAGC CGACCTCGT GCTGCCGCGC GGGCCGTCGC CGACGCCGGG

+1 S G H V H A S D G A A P R A G L A W S P C S R R Q L
Zinc-binding Motif

Metalloproteinase Domain

825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGACGTGC
GTCGCCTGTG CACTACCGAA GCCTGCCGCG CGCGGGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCCGTCGACG

+1 L S L L S A G R A R C V W D P P R P Q P G S A G H P F
Metalloproteinase Domain

905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCG GGTCCGCGGG GCACCCGCGG
ACTCGGACGA GTCGCGTCTT GCCCGCGCGA CGACACCCCT GGCGGGCGCC GGAGTTGGGC CCAGGCGCCC CGTGGGCGGG

+1 D A Q P G L Y Y S A N E Q C R V A F G P K A V A C T F
Disintegrin Domain

985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTGCGCCCC AAGGCTGTG CCTGCACCTT
CTACGCGTGC GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA

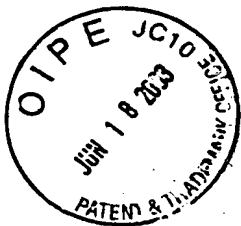


FIG. 3D

+1 A R E H L D M C Q A L S C H T D P L D Q S S C S F L
Disintegrin Domain

1065 CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCTGCT
GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGAGC GTGTGTCTGG GCGACCTGGT TTCGTCGACG TCGGCTGAGC

+1 L V P L L D G T E C G V E K W C S K G R C R S L V E L
Disintegrin Domain

1145 TCGTTCCTCT CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCTCC AAGGGTCTGT GCCGCTCCCT GGTGGAGCTG
AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TTTCCAGCGA CGGCGAGGGA CCACCTCGAC

+1 T P I A A V H G R W S S H G P R S P C S R S C G G G
Heparin-binding Motif

Thrombospondin Submotif

1225 ACCCCCATAG CAGCAGTGCA TGGGCGCTGG TCTAGCTGGG GTCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGCTG
TGGGGGTATG GTCGTCACGT ACCCGGACCC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCCTCCACA

+1 V T R R R Q C N N P R P A F G G R A C V G A D L Q A
Thrombospondin Submotif

1305 GGTACCAGG AGGCGGCAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGTGAC CTCACGGCCG
CCAGTGGTCC TCCGCCGTCA CGTTGTGGG GTCTGGACGG AAACCCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC

+1 E M C N T O A C E K T Q L E F M S Q Q C A R T D G C P
Thrombospondin Submotif

1385 AGATGTGCAA CACTCAGGCC TGCAGAAGA CCCAGCTGGA GTTCATGTG CACAGTGCG CCAGGACCGA CGGCCAGCCG
TCTACACGTT GTGAGTCCGG ACGCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTACGC GGTCTGGCT GCCGGTCCGG

+1 L R S S P G G A S F Y H W G A A V P H S Q G D A L C R
1465 CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCAG
GACCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTGACCC CACGACGACA TGGTGTGTCG GTTCCCTAC GAGACACGT

+1 H M C R A I G E S F I M K R G D S F L D G T R C H P
1545 ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
TGTGTACAG GCCCGGTAAC CGCTCTCGAA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATACGGT

+1 S G P R E D G T L S L C V S G S C R T F G C D G R M D
1625 GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTGC GGGCAGCTGC AGGACATTTG GCTGTGATGG TAGGATGGAC
CACCGGGGGC CCTCCTGCC TGGGACTCGG ACACACACAG CCCGTGACG TCCTGTAAAC CGACACTACC ATCTACCTG

+1 S Q Q V W D R C Q V C G G D N S T C S P R K G S F T A
1705 TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
AGGGTCGTCC ATACCCTGTC CACGGTCCAC ACACCACCC TGTGTCTGT CACGTCCGGT GCCTTCCCA GAAAGTGTG

+1 G R A R E Y V T F L T V T P N L T S V Y I A N H R P
1785 TGGCAGAGCG AGAGAATATG TCACGTTTCT GACAGTTACC CCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
ACCGTCTCGC TCTCTTATAC AGTGCAAAGA CTGTCAATGG GGGTTGGACT GGTCACAGAT GTAACGGTTG GTGTCCGGAG

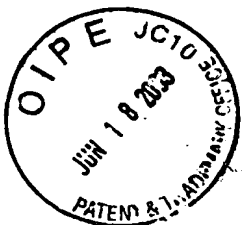


FIG. 3E

+1 L F T H L A V R I G G R Y V V A G K M S I S P N T T
1965 TCCTCACACA CTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCTAA CACCACTTAC
AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATT

+1 P S L L E D G R V E Y R V A L T E D R L P R L E E F
1945 CCCTCCCTCC TGGAGGATGG TCGTGTGAG TACAGAGTGG CCCTACCGA GGACCGGCTG CCGGCTGG AGGAGATCCG
GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTACCC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTGTAGGT

+1 I W G P L Q E D A D I O V Y R R Y G E E Y G N L T F
2025 CATCTGGGGA CCCTCCAGG AAGATGCTGA CATCCAGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCGCG
GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGTCTCT CATACCGTGT GAGTGGGCGG

+1 P D I T F T Y F O P K P R O A W V W A A V R G P C S
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCGTGGGTG TGGGCCGCTG TCGTGGGCC CTGCTGGGTG
GTCTGTAGTG GAAGTGGATG AAGGTCCGAT TCGGTGCCGT CCGGACCCAC ACCCGGGGAC ACCGACCCGG GACGAGGCAE

+1 S C G A G L R W V N Y S C L D O A R K E L V E T V D
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGTGGC TGGACAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
TCGACACCCG GTCCGAGCG GACCCATTG ATGTGACGG ACCTGGTCCG GTCTTCTCTC AACCACTCT GACAGGTCAE

+1 Q G S Q O P P A W P E A C V L E P C P P Y W A V G E
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCGTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGCT
GGTTCCTCG GTCTCGGTG GTGCAACCG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCCTGA

+1 F G P C S A S C G G G L R E R P V R C V E A O G S L L
2345 TCGGCCCCATG CAGCGCTCC TGTGGGGTG GCCTGCGGA GCGGCCAGTG CGTGGCTGG AGGCCAGGG CAGCCTCTG
AGCCGGGTAC GTGCGGAGG ACACCCAC CCGACGCCCT CGCCGGTAC GCGACGCACC TCCGGGTCC GTGCGAGGAC

+1 K T L P P A R C R A G A Q Q P A V A L E T C N P Q P C
2425 AAGACATTG CCGAGCCCG GTGCAGAGCA GGGGCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCGAGCCCTG
TTCTGTAACG GGGGTCCGGC CAGTCTCGT CCGCGGTG TCGTGCACA CCGGACCTT TGGACGTTG GGTGCGGGAC

+1 P A R W E V S E P S S C T S A G G A G L A L E N E T
2505 CCCTGCCAGG TGGAGGTGT CAGAGCCAG CTCATGCACA TCAGTGGTG GAGCAGGCT GGCCTGGAG AACGAGACCT
GGGACGGTCC ACCCTCCACA GTCTCGGGT GAGTACGTT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA

+1 C V P G A D G L E A P V T E G P G S V D E K L P A P E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGAAGA GGGGCTGGC TCCGTAGATG AGAAGCTGCC TGCCCTGAG
CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCGGAGCCG AGGCATCTAC TCTCGACGG ACGGGGACTC

+1 P C V G M S C P P G W G H L D A T S A G E K A P S P W
2665 CCCTGTGTG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGG GAGAAGGCTC CCTCCCCATG
GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCGGTAG ACCTACGGT GAGACGTCC CTCTCCGAG GGAGGGGTAC

+1 G S I R T G A Q A A H V W T P A A G S C S V S C G R
2745 GGGCAGCATC AGGACGGGG CTCAAGTGC ACAGTGTGG ACCCTGCGG CAGGGTCTG CTCGTCTCC TCGGGCGAG
CCGTCGTAG TCCTGCCCC GAGTTCGAG TGTGCACAC TGGGACGCC GTCCAGCAC GAGGCAGAGG ACGCCCGCTC

+1 G L H E L R F L C M D S A L R V P V Q E E L C G L A S
2825 GTCTGATGA GCTGCTTTC CTGTGCATG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTG CCTGGCAAGC
CAGACTACCT CGACGCAAG GACACGTACC TGAGACGGGA GTCCACGGA CAGGTCTTC TCGACACACC GGACCGTTCC

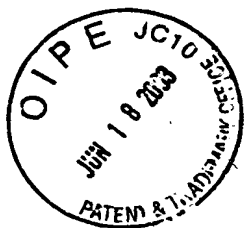


FIG. 3F

+1 K P G S R R E V C Q A V P C F A R W Q Y F L A A I C
2905 AAGCCTGGGA GCCGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGGGGG CCGGAGGCT
TTCGGACCCCT CGGCGCGCCT CCAGACGGTC CGACAGGGGA CGGGACGAGC CACCGTCATG TTCGACCGCG GGACCTGGGA

+1 S C G R G V V R R I L Y C A R A H G E D D G E E I L
2985 GAGCTGTGGG AGAGGGGTCG TCGGAGGAT CCGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCGTGT
CTCGACACCC TCTCCCCAGC ACGCCTCCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA

+1 L D T Q C Q G L P R P E P Q E A C S L E P C P P R W Y
3065 TGGACACCCA GTGCCAGGGG CTGCCTCGCC CGGAACCCCA GGAGGCTGCG AGCCTGGAGC CCGCCCGACC TAGGTGGAAA
ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCGTTGGGT CCGCGGAGC TCGGACCTCG GGACGGGTGG ATCCAGCTGT

+1 V M S L G P C S A S C G L G T A R R S V A C V Q L C I
3145 GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGAGCA
CAGTACAGGG AACCGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TCGGAGCCAC CGGACACAGC TCGAGCTTGT

+1 G Q D V E V D E A A C A A L V R P E A S V F C L I A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGGGCG CCGAGGCGAG TGTCCTCTGT CTCATTGGCG
TCCGGTCTCG CACCTCCACC TGCTCCGCGG GACACGCGCG GACCACGCGG GGCTCCGGTC ACAGGGGACA GAGTAACGGC

+1 D C T Y R W H V G T W M E C S V S C G D G I O R R R C
Thrombospondin Submotif
3305 ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
TGACGTGGAT GCGGACCGTA CAACCGTGA CTAACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTGCG GCGCGCACTG

+1 T C L G P Q A Q A P V P A D F C Q H L P K P V T V R I
Thrombospondin Submotif
3385 ACCTGCCTCG GACCCAGGC CCAGGCGCCT GTGCCAGTG ATTTCTGCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
TGGACGAGC CTGGGTCCG GGTCCGCGGA CACGGTCGAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACT

+1 C H A G P C V G Q G T P S L V P H E E A A A P G R T
Thrombospondin Submotif
3465 CTGCTGGGCT GGGCCCTGTG TGGGACAGG TACGCCAGC CTGGTGCCCC ACGAAGAAGC CGTGCTCCA GGACGGACCA
GACGACCGA CCGGGGACAC ACCCTGTCCC ATGCGGGTCC GACCACGGGG TGCTTCTCG GCGACGAGGT CCGCTCTGGT

+1 T A T P A G A C G R Q H L E P T G T I D M R G P G Q A
3545 CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCCAACAGGA ACCATTGACA TCGAGGCCCC AGGGCAGGCA
GTCGGTGGGG ACGACCAAGG ACACCGTCCG TCGTGGAAC TCGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCGTCCCG

+1 D C A V A I G R P L G E V V T L R V L E S S L N C S A
3625 GACTGTGCAG TGGCCATTGG GCGGCCCTC GGGGAGGTGG TGACCTCCG CGTCTTGAG AGTTCTCTCA ACTGCAGTGC
CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAATC TCAAGAGAGT TGACGTCACT

+1 G D M L L L W G R L T W R K M C R K L L D M T F S S
3705 GGGGGACATG TTGCTGCTTT GGGGCGGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGTCCA
CCCCCTGTAC AACGACGAAA CCGCGGCCGA GTGGACCTCC TTCTACACGT CCTTCGACAA CCGTACTGA AAGTCGAGGT

+1 K T N T L V V R Q R C G R P G G G V L L R Y G S Q L A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGTGCG GGTATGGGAG CCAGCTTGGT
TCTGGTGTG CGACCAACAC TCCGTCCGA CGCCGCGCGG TCCTCCACCC CACGACGAGC CCATACCCCTC GGTCGAACCA

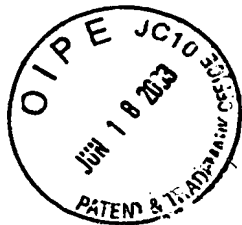


FIG. 3G

+1 P E T F Y R E C D M Q L F G P W G E I V S P S L S F A
3865 CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCTCGC TGAGTCCAGC
GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTTG

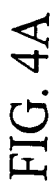
+1 T S N A G G C R L F I N V A P H A R T A I H A L A T
3945 CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
GTGCTCATTG CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

+1 N M G A G T E G A N A S Y I L I R D T H S L R T T A F
4025 ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
TGTACCCGCG ACCCTGGCTC CCTCGGTTAG GGTCGATGA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTGGCAAG

+1 H G Q Q V L Y W E S E S S O A E M E F S E G F L K A I
4105 CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

+1 A S L R G Q Y W T L Q S W V P E M Q D P Q S W K G K
4185 GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCTGG AAGGGAAGG
CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCTGGG AGTCAGGACC TTCCCTTGG

+1 E G T
4265 AAGGAACC
TTCCTTGG



Percent Homology

[illegible]

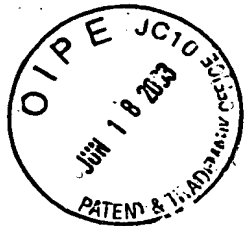
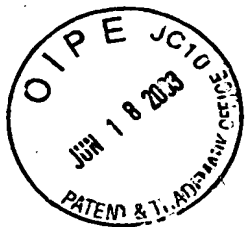


FIG. 4B

541
HADAMTS-4 (AB014588) (429) EAP--LHEBVTFRG--KDYVDRGQULTEGDSRHC--QLPPPCALMGSGHNLNCHAMC 600
HADAMTS-5 (AF142099) (476) RKO--ILGEEFEG--QTGATONINLGGSEYSVCE--GNDVYKALMGCAVVRQOMV
HADAMTS-1 (AF060152) (451) QNP--IQAGGDRG--TSKNNRQOTFSGEDSKHP--DRASTETINCTGTSGVVLV
HADAMTS-8 (AF060153) (431) GNA--LPFTTGEGSMALGIDOCQROIFETEFRCBNTSAQDVGAGQWGH-TDCAEPLG
HADAMTS-2 (AJ003125) (471) FTHDWPATF--QHEG--LHKSNNEXRFDGSLGYNNETAFRTFDEKQMGES-HPDNPYFE
(213) RP-----
M1-HPD
Consensus (541) A LP LPG YDA QC TFGPD HCP D CA LMC G C



~~FIG. 1~~ FIG. 1A

CCGGGTCGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG
5 CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCCTCCCCTCTGTGTGGC
CGGAATCCTTGCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA
GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC
TAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCCGGG
CTGCAGGCCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA
10 GGCTCACCAGGAGGACACAGAGCGCTATGTGCTCACCAACCTCAACATCGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGCTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG
CTGACCTGGTCTCTATATCACTAGGTTTGACCTGGAGTTGCCTGATGGTAACGGGCAG
15 GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATT
CCGAGGACACTGGCTTCGACCTGGGAGTCACCATGCCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCACGACGGCGCGCCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA
TGGCTTCGGACGGCGCGCGCCCCGCGCCGGCCTCGCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCGCG
20 GGCCTCAACCCGGGTCCGCGGGGCACCCGCGGATGCGCAGCCTGGCCTCTACTACA
GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTGCGCTGCACCTTCGC
CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGCAGCCGCCTCCTCGTTCCTCTCCTGGATGGGACAGAATGTGGCGTGGAGA
AGTGGTGCTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCATAGCAGCAGT
25 GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA
GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCAGACCTGCCTTTGGGGGGCGT
GCATGTGTTGGTGCTGACCTCCAGGCCGAGATGTGCAACACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTCATGTCGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
CTCCCCCTGGCGGCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG
30 GATGCTCTGTGCAGACACATGTGCCGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG
GAGACAGCTTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCCGGGAGGACGGGA
CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTTGGCTGTGATGGTAGGATGGA
CTCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGGACAACAGCACGTGCAGC
CCACGGAAGGGCTCTTTCACAGCTGGCAGAGCGAGAGAATATGTCACGTTTCTGACAGT
35 TACCCCAACCTGACCAGTGTCTACATTGCCAACACAGGCCTCTCTTACACACTTGG
CGGTGAGGATCGGAGGGCGCTATGTGCTGGCTGGGAAGATGAGCATCTCCCCTAACAC
CACCTACCCCTCCCTCCTGGAGGATGGTGTGTCGAGTACAGAGTGGCCCTCACCGAG

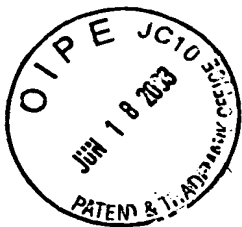


FIG. 1B

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAACTACAGCTGCCTG
5 GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCTGCGGGAGCGGCCAGTGCGC
TGCCTGGAGGCCAGGGCAGCCTCCTGAAGACATTGCCCCAGCCCGGTGCAGAGCA
GGGGCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
10 AGGTGGGAGGTGTCAGAGCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGAAGGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCCTGAGCCCTGTGTGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG
15 TCGTGCTCCGTCTCCTGCGGGCAGAGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGGCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTGCTGCGGAGGATCCTGTATTGTGCCCCG
GGCCCATGGGGAGGACGATGGTGAAGAGATCCTGTTGGACACCCAGTGCCAGGGGCT
20 GCCTCGCCCGGAACCCCAGGAGGCCTGCAGCCTGGAGCCCTGCCCACCTAGGTGGAA
AGTCATGTCCCTTGCCCCATGTTCCGGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG
25 CCGGCGTGACACCTGCCTCGGACCCCAGGCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGGCCCTCGGGGAGGT
30 GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAAGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA
35 ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCATGGGCAGCAGGTGCTCTACTG

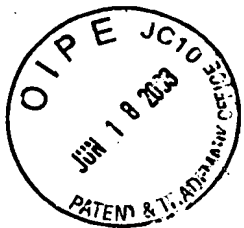


FIG. 1C

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

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100-12-0000
100-12-0000

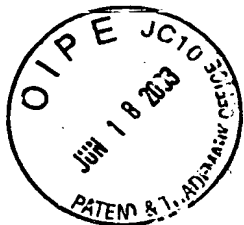
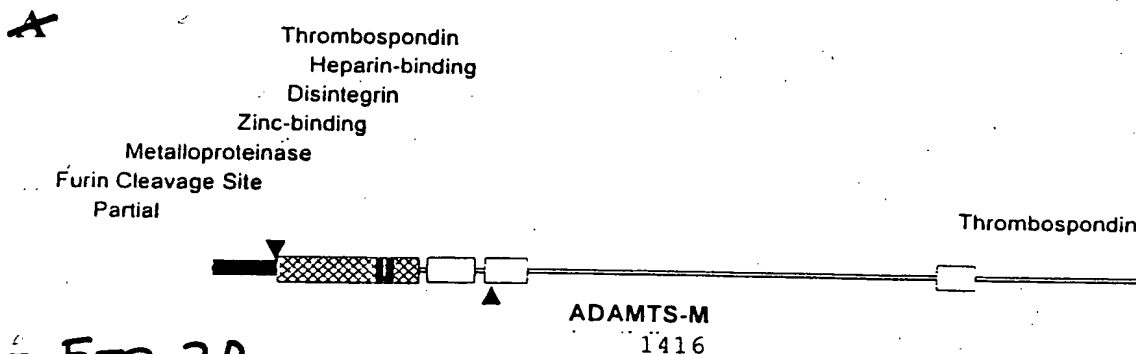


FIG. 3A

Domain structure of ADAMTS-M and translated nucleic acid sequence. ~~Figure-3~~ **FIG. 3A** Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding domain (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). **FIGS. 3B-3G** ADAMTS-M nucleotide sequence with translated amino acid sequence above.



B FIG. 3B

```
+1 P G R P T R P K A P S H S A P L L G L A L L R M H Q R
                                         Partial Prodomain
-----
25 CCGGGTCGAC CCACGCTCC GAAGGCCCCC TCTACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGCACCAGCG
   GGCCAGCTG GGTGCGCAGG CTTCCGGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCGC
-----
+1 H P R A R C P P L C V A G I L A C G F L L G C W S F
                                         Partial Prodomain
-----
105 TCACCCCGG GCAAGATGCC CTCCCCTCTG TGTGGCCGGA ATCCTTGCTT GTGGCTTTCT CCTGGGCTGC TGGGGACCCG
   AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACGGA CACCGAAAGA GGACCCGACG ACCCTGGGA
-----
+1 S H F Q Q S C L Q A L E P Q A V S S Y L S P G A P L K
   Partial Prodomain
-----
185 CCCATTCCA GCAGATTGT CTTAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTTAAAA
   GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAAC CGGGACCACG AGGGAATTTT
-----
+1 G R P P S P G F Q R Q R Q R R A A G G I L H L E L
   Furin Cleavage Site (Motif)
-----
Partial Prodomain                               Metalloproteinase Domain
-----
265 GGCCGCCCTC CTTCCCTGG CTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
   CCGCGGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA
-----
+1 L V A V G P D V F Q A H Q E D T E R Y V L T N L N I
                                         Metalloproteinase Domain
-----
345 GCTGGTGGCC GTGGGCCCGG ATGTCTTCCA GGCTCACCAG GAGGACACAG AGCGCTATGT GCTCACCACG CTCAACATCG
   CGACCACCGG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
```



FIG. 3C

+1 G A E L L R D P S L G A Q F R V H L V K M V I L T E F
Metalloproteinase Domain

425 GGGCAGAACT GCTTCGGGAC CCGTCCCTGG GGGCTCAGTT TCGGGTGAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCACGTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

+1 E G A P N I T A N L T S S L L S V C G W S Q T I N P E
Metalloproteinase Domain

505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCCCTGA
CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT

+1 D D T D P G H A D L V L Y I T R F D L E L P D G N E
Metalloproteinase Domain

585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCTCTAT ATCACTAGGT TTGACCTGGA GTTGCCTGAT GGTAACCGGC
CCTGCTGTGC CTAGGACCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCGC

+1 Q V R G V T Q L G G A C S P T W S C L I T E D T G F E
Metalloproteinase Domain

665 AGGTGCGGGG CGTACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCTATTA CCGAGGACAC TGGCTTCGAC
TCCACGCCCC GCAGTGGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCCTGTG ACCGAAGCTG

+1 L G V T I A H E I G H S F G L E H D G A P G S G C G F
Zinc-binding Motif

Metalloproteinase Domain

745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCCC
GACCCTCAGT GGTAACGGGT ACTCTAACCC GTGTCGAAGC CGGACCTCGT GCTGCCGCGC GGGCCGTGCG CGACGCGGGG

+1 S G H V M A S D G A A P R A G L A W S P C S R R Q L
Zinc-binding Motif

Metalloproteinase Domain

825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGCAGCTGC
GTCGCCTGTG CACTACCGAA GCCTGCCGCG GCGCGGGGCG CGGCCGAGC GGACCAGGGG GACGTCGGCG GCCGTCGACG

+1 L S L L S A G R A R C V W D P P R P Q P G S A G H P F
Metalloproteinase Domain

905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTTGGA CCCGCCGCGG CCTCAACCCG GGTCCGCGGG GCACCCGCGG
ACTCGGACGA GTCGCGTCTT GCGCGCGCGA CGCACACCCT GGGCGGCGCC GGAGTTGGGC CCAGGCGCCC CGTGGGCGGC

+1 D A Q P G L Y Y S A N E Q C R V A F G P K A V A C T F
Disintegrin Domain

985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTCGGCCCC AAGGCTGTG CCTGCACCTT
CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA

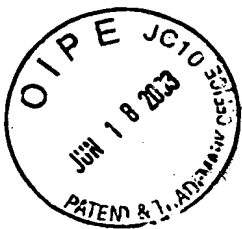


FIG. 30

+1 A R E H L D M C Q A L S C H T D P L D Q S S C S F L
Disintegrin Domain

1065 CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCTGCT
GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGTCTGG GCGACCTGGT TTCGTCGACG TCGGTGGAGG

+1 L V P L L D G T E C G V E K W C S K G R C R S L V E L
Disintegrin Domain

1145 TCGTTCCTCT CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCTCC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TCCCCAGCGA CGGCGAGGGA CCACCTGAGC

+1 T P I A A V H G R W S S W G P R S P C S R S C G G G V
Heparin-binding Motif

Thrombospondin Submotif

1225 ACCCCCATAG CAGCAGTGCA TGGGCGCTGG TCTAGCTGGG GTCCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
TGGGGGTATC GTCGTCACGT ACCCGCGACC AGATCGACCC CAGGGGGCTT AGGAACGAGG GCGAGGACGC CTCCTCCACA

+1 V T R R R Q C N N P R P A F G G R A C V G A D L Q A
Thrombospondin Submotif

1305 GGTACCAGG AGGCGGCAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGCGC
CCAGTGGTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCCG CAGTACACA ACCACGACTG GAGGTCCGGC

+1 E M C N T Q A C E K T Q L E F M S Q Q C A R T D G Q P
Thrombospondin Submotif

1385 AGATGTGCAA CACTCAGGCC TGCAGAAGA CCCAGCTGGA GTTCATGTG CAACAGTGCG CCAGGACCGA CGGCCAGCCG
TCTACACGTT GTGAGTCCGG ACCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTACGC GGTCCTGGCT GCCGGTCGGC

+1 L R S S P / G G A S F Y H W G A A V P H S Q G D A L C R
1465 CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCAG
GACCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTGACCC CACGACGACA TGGTGTGTCG GTTCCCTTAC GAGACACGTC

+1 H M C R A I G E S F I M K R G D S F L D G T R C M P
1545 ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
TGTGTACAG GCCCGGTAAC CGCTCTCGAA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATACGGTT

+1 S G P R E D G T L S L C V S G S C R T F G C D G R M D
1625 GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTGTC GGGCAGCTGC AGGACATTTG GCTGTGATGG TAGGATGGAC
CACCAGGGGC CCTCCTGCCC TGGGACTCGG ACACACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCTACCTG

+1 S Q Q V W D R C Q V C G G D N S T C S P R K G S F T A
1705 TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
AGGGTCGTCC ATACCCTGTC CACGGTCCAC ACACCACCC TGTGTGCTG CACGTCGGGT GCCTTCCCGA GAAAGTGTG

+1 G R A R E Y V T F L T V T P N L T S V Y I A N H R P
1785 TGGCAGAGCG AGAGAATATG TCACGTTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
ACCGTCTCGC TCTCTTATAC AGTGCAAAGA CTGTCAATGG GGGTTGGACT GGTACAGAT GTAACGGTTG GTGTCCGGAG

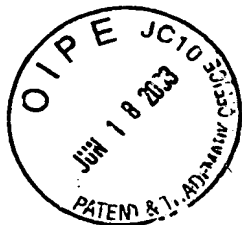


FIG. 3E

+1 L F T H L A V R I G G R Y V V A G K M S I S P N T T
1965 TCTTCACACA CTTGGCGGTG AGGATCGGAG GCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCTAA CACCACTAC
AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGAT

+1 P S L L E D G R V E Y R V A L T E D R L P R L E E : F
1945 CCCTCCCTCC TGGAGGATGG TCGTGTGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCCTGG AGGAGATCCG
GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTCTAGG

+1 I W G P L Q E D A D I Q V Y R R Y G E E Y G N L T F
2025 CATCTGGGGA CCCTCCAGG AAGATGCTGA CATCCAGGT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCCG
GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCCTCT CATACCGTGT GACTGGCGCG

+1 P D I T F T Y F Q P K P R Q A W V W A A V R G F C S V
2105 CAGACATCAC CTTACCTAC TTCCAGCCTA AGCCACGGCA GCGCTGGGTG TGGGCGCTG TCGTGGGCC CTGCTCGGTG
GTCTGTAGTG GAAGTGGATG AAGGTGGAT TCGGTGCCGT CCGGACCCAC ACCCGCGAC ACGACCCCG GACGAGCCAT

+1 S C G A G L R W V N Y S C L D Q A R K E L V E T V Q :
2185 AGCTGTGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGG CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
TCGACACCCC GTCCCGACGC GACCCATTG ATGTGACGCG ACCTGGTCCG GTCTTCCTC AACCACCTCT GACAGSTCAT

+1 Q G S Q Q P P A W P E A C V L E P C P P Y W A V G D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCTGC GTGCTCGAAC CTGCCCCTCC CTACTGGGCG GTGGGAGACT
GGTTCCCTCG GTCGTGGGTG GTCGCACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCTCTGA

+1 F G P C S A S C G G G L R E R P V R C V E A Q G S L L
2345 TCGGCCCATG CAGCGCTCC TGTGGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCAGGG CAGCCTCCTG
AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTAC GCGACGCACC TCCGGGTCCG GTCGGAGGAC

+1 K T L P P A R C R A G A Q Q P A V A L E T C N P Q P C
2425 AAGACATTGC CCCCAGCCCG GTGCAGAGCA GGGGCCAGC AGCCAGCTGT GCGCTGGAA ACCTGCAACC CCCAGCCCTG
TTCTGTAACG GGGGTCCGGC CAGGTCTCGT CCCCAGGTG TCGGTGACA CCGGACCTT TGGACGTTG GGGTCCGGAC

+1 P A R W E V S E P S S C T S A G G A G L A L E N E T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG CTCATGCACA TCAGTGGTG GAGCAGGCT GGCCTGGAG AACGAGACCT
GGGACGGTCC ACCCTCCACA GTCTCGGGTC GAGTACGTGT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA

+1 C V P G A D G L E A P V T E G P G S V D E K L P A P E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTACTGA GGGGCTGGC TCCGTAGATG AGAAGTGGC TGCCCTGAG
CACAGGTCC CCGTCTACCG GACCTCCGAG GTCAGTACT CCCCAGGACG AGGCATCTAC TCTTCGACG ACGGGGACTC

+1 P C V G M S C P P G W G H L D A T S A G E K A P S P W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CTCCCCATG
GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCGGTAG ACCTACGCTG GAGACGTCCC CTCTCCGAG GGAGGGGTAC

+1 G S I R T G A Q A A H V W T P A A G S C S V S C G R
2745 GGGCAGCATC AGGACGGGG CTCAAGCTGC ACACGTGTG ACCCTGCGG CAGGGTCGTG CTCCGTCTCC TGCGGGCGAG
CCCGTCGTAG TCCTGCCCCC GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCAGCAC GAGGCAGAGG ACGCCCGCTC

+1 G L M E L R F L C M D S A L R V P V Q E E L C G L A S
2825 GTCTGATGGA GCTGCGTTT CTGTGCATGG ACTGTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCACGGA CAGGTCTTC TCGACACACC GGACCGTTCG

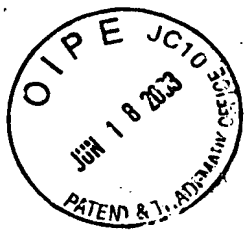


FIG. 3F

+1 K P G S R R E V C Q A V P C F A R W Q Y K L A A D D
2905 AAGCCTGGGA GCCGGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGGGCG CTTGACGCTG
TTCGGACCCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA GGGGACGAGC CACCGTCATG TTCGACCGCC GGACCTGCGA

+1 S C G R G V V R R I L Y C A R A H G E D D G E E L
2985 GAGCTGTGGG AGAGGGGTG TGGGAGGAT CCTGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCGCTG
CTCGACACCC TCTCCCCAGC ACGCCTCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA

+1 L D T Q C Q G L P R P E P Q E A C S L E P C P P R W F
3065 TGGACACCCA GTGCCAGGG CTGCCCTGCC CGAACCCCA GGAGGCCTGC AGCCTGGAGC CCTGCCCACT TAGGTGAAAA
ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGGT CCTCCGGAGC TCGGACCTCG GGACGGGTGG ATCCACCTTT

+1 V M S L G P C S A S C G L G T A R R S V A C V Q L D I
3145 GTCATGTCCC TTGGCCCATG TTCGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGACCA
CAGTACAGGG AACCGGGTAC AAGCCGGTGC ACACCGGAAC CGTGACGATC TCGGAGCCAC CGGACACACG TCGAGCTGCT

+1 G Q D V E V D E A A C A A L V R P E A S V P C L I A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGCGGC CCGAGGCCAG TGTCCTCTGT CTCATTGCGG
TCCGGTCTG CACCTCCACC TGCTCCGCCG GACACGCCGC GACCACGCCG GGCTCCGGTC ACAGGGGACA GAGTAACCGG

+1 D C T Y R W H V G T W M E C S V S C G D G I Q R R R D
Thrombospondin Submotif
3305 ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
TGACGTGGAT GCGGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTGCG GCGCCGACTG

+1 T C L G P Q A Q A P V P A D F C Q H L P K P V T V R E
Thrombospondin Submotif
3385 ACCTGCCTCG GACCCAGGC CCAGGCGCCT GTGCCAGCTG ATTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTGCAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACC

+1 C W A G P C V G Q G T P S L V P H E E A A A P G R T
Thrombospondin Submotif
3465 CTGCTGGGCT GGGCCCTGTG TGGGACAGGG TACGCCAGC CTGGTGCCCC ACGAAGAAGC CGCTGCTCCA GGACGGACCA
GACGACCGCA CCCGGGACAC ACCCTGTCCC ATGCGGGTGC GACCACGGGG TGCTTCTTCG GCGACGAGGT CCGCTGCTGG

+1 T A T P A G A C G R Q H L E P T G T I D M R G P G Q A
3545 CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCCAACAGGA ACCATTGACA TCGGAGGCCC AGGGCAGGCA
GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGGAAC TCGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCGTCCGT

+1 D C A V A I G R P L G E V V T L R V L E S S L N C S A
3625 GACTGTGCAG TGGCCATTGG GCGGCCCTC GGGGAGGTGG TGACCTCCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACCT TCAAGAGAGT TGACGTCAAG

+1 G D M L L L W G R L T W R K M C R K L L D M T F S S
3705 GGGGACATG TTGCTGCTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
CCCCCTGTAC AACGACGAAA CCCCAGGCGA GTGGACCTCC TTCTACACGT CTTTCGACAA CCTGTACTGA AAGTCGAGGT

+1 K T N T L V V R Q R C G R P G G G V L L R Y G S Q L A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
TCTGGTTGTG CGACCAACAC TCCGTGCGGA CGCCCGCCGG TCCTCCACCC CACGACGAGC CCATACCTC GGTGCAACCA



FIG. 3G

+1 P E T F Y R E C D M Q L F G P W G E I V S P S L S F A
3865 CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCTGGGG TGAAATCGTG AGCCCTCGC TGAGTCCAGT
GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTGG

+1 T S N A G G C R L F I N V A P H A R I A I H A L A T
3945 CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

+1 N M G A G T E G A N A S Y I L I R D T H S L R T T A F
4025 ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCCTTC
TGACCCGCG ACCCTGGCTC CCTCGGTTAC GGTCGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTGCAAG

+1 H G Q Q V L Y W E S E S S Q A E M E F S E G F L K A I
4105 CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

+1 A S L R G Q Y W T L Q S W V P E M Q D P Q S W K G K
4185 GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCTGG AAGGGAAAGG
CCGGTCGGAC GCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCTTTGG

+1 E G T
4265 AAGGAACC
TTCCTTGG

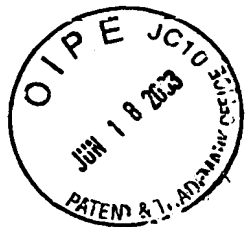


FIG. 4B

541 600
HADAMTS-4 (AB014588) (429) EAP--LHEVTFE--KDYA DRGQLNCEPSRUCP--QLPPPCRAIMCSGHLNCHAMG
HADAMTS-5 (AF142099) (476) RKO--ILGEEDEE--OT--TQCNLEFDEYSYV--GMVPRKMGAVVRQOMV
HADAMTS-1 (AF060152) (451) ONP--IQEAGDGG--TSK--NR--OF--EESK--DAASTETITCTGTSCVLVE
HADAMTS-8 (AF060153) (431) GNA--LPHTGEGRNALGOLDQGRQIETEPFRCEPNTSAQVRAQLMCH-TDGAEPLE
HADAMTS-2 (AJ003125) (471) FHDWPADE-QHGG--LHESMNEE--RFDE--LSYMMCTAFTTDPKQKES-HPDNPYFE
M1-MPD (213) RP-----
Consensus (541) A LP LPG YDA QC TFGPD HCP D CA LWC G C